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=> s (conotoxin? or conopeptide?) (s) ((alpha (w) 1) (s) (adrenergic (w) receptor# or adrenoceptor#))
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L2 0 FILE ADISINSIGHT
L3 0 FILE ADISNEWS
L4 0 FILE AGRICOLA
L5 0 FILE ANABSTR
L6 1 FILE AQUASCI
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L10 0 FILE BIOTECHDS
L11 0 FILE BIOTECHNO
L12 1 FILE CABA
L13 0 FILE CANCERLIT
L14 8 FILE CAPLUS
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L19 0 FILE CROPB
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L21 1 FILE DISSABS
L22 5 FILE DGENE
L23 0 FILE DRUGB
L24 0 FILE DRUGMONOG2
L25 0 FILE IMSDRUGNEWS
L26 1 FILE DRUGU
L27 0 FILE IMSRESEARCH
L28 0 FILE EMBAL
L29 16 FILE EMBASE
L30 1 FILE ESBIOBASE
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L35 0 FILE FSTA
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L41 0 FILE KOSMET
L42 1 FILE LIFESCI

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L48           0 FILE OCEAN
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L57          11 FILE SCISEARCH
L58           0 FILE SYNTHLINE
L59           8 FILE TOXCENTER
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L61           0 FILE USPAT2
L62           0 FILE VETB
L63           0 FILE VETU
L64           1 FILE WPIDS

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L66  ANSWER 1 OF 32  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:684944  CAPLUS
DOCUMENT NUMBER:          139:301294
TITLE:                    Allosteric α1-adrenoreceptor antagonism by
                          conopeptide ρ-TIA
AUTHOR(S):                Sharpe, Iain A.; Thomas, Linda; Loughnan, Marion;
                          Motin, Leonid; Palant, Elka; Croker, Daniel E.;
                          Alewood, Dianne; Chen, Songhai; Graham, Robert M.;
                          Alewood, Paul F.; Adams, David J.; Lewis, Richard J.
CORPORATE SOURCE:         Institute of Molecular Bioscience and the School of
                          Biomedical Sciences, The University of Queensland, St.
                          Lucia, Queensland, 4072, Australia
SOURCE:                   Journal of Biological Chemistry (2003), 278(36),
                          34451-34457
                          CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER:                American Society for Biochemistry and Molecular
                          Biology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   A peptide contained in the venom of the predatory marine snail Conus
     tulipa, ρ-TIA, has previously been shown to possess
     α1-adrenoreceptor antagonist activity.  Here, the authors further
     characterize its pharmacol. activity as well as its structure-activity
     relationships.  In the isolated rat vas deferens, ρ-TIA inhibited
     α1-adrenoreceptor-mediated increases in cytosolic Ca2+ concentration that
     were triggered by norepinephrine, but did not affect presynaptic
     α2-adrenoreceptor-mediated responses.  In radioligand binding assays
     using [125I]HEAT, ρ-TIA displayed slightly greater potency at the
     α1B than at the α1A or α1D subtypes.  Moreover, although
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it did not affect the rate of association for [3H]prazosin binding to the α1B-adrenoreceptor, the dissociation rate was increased, indicating non-competitive antagonism by ρ-TIA. N-terminally truncated analogs of ρ-TIA were less active than the full-length peptide, with a large decline in activity observed upon removal of the fourth residue of ρ-TIA (Arg4). An alanine walk of ρ-TIA confirmed the importance of Arg4 for activity and revealed a number of other residues clustered around Arg4 that contribute to the potency of ρ-TIA. The unique allosteric antagonism of ρ-TIA resulting from its interaction with receptor residues that constitute a binding site that is distinct from that of the classical competitive α1-adrenoreceptor antagonists may allow the development of inhibitors that are highly subtype selective.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 2 OF 32 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:274913 SCISEARCH
THE GENUINE ARTICLE: 656LZ
TITLE: An examination of calcium current function on heterotopic neurons in hippocampal slices from rats exposed to methylazoxymethanol
AUTHOR: Calcagnotto M E; Baraban S C (Reprint)
CORPORATE SOURCE: Univ Calif San Francisco, Dept Neurol Surg, Epilepsy Res Lab, Box 0520, 513 Parnassus Ave, San Francisco, CA 94143 USA (Reprint); Univ Calif San Francisco, Dept Neurol Surg, Epilepsy Res Lab, San Francisco, CA 94143 USA; Univ Calif San Francisco, Grad Program Neurosci, San Francisco, CA 94143 USA
COUNTRY OF AUTHOR: USA
SOURCE: EPILEPSIA, (MAR 2003) Vol. 44, No. 3, pp. 315-321. Publisher: BLACKWELL PUBLISHING INC, 350 MAIN ST, MALDEN, MA 02148 USA. ISSN: 0013-9580.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 57
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Purpose: To study voltage-dependent calcium currents (VDCCs) on hippocampal heterotopic neurons by using whole-cell patch-clamp techniques in brain slices prepared from methylaxozymethanol (MAM)-exposed rats.

Methods: Whole-cell voltage-clamp recordings were obtained from visually identified neurons in acute brain slices by using an infrared differential interference contrast (IR-DIC) video microscopy system. Heterotopic neurons were compared with normotopic pyramidal cells in hippocampal slices from MAM-exposed rats or CA1 pyramidal neurons in slices from controls.

Results: Heterotopic neurons expressed a prominent VDCC, which exhibited a peak current maximum around -30 mV (holding potential, -60 mV) and an inactivation time constant of 48.2 +/- 2.4 ms (n = 91). VDCC peak current and inactivation time constants were similar for normotopic (n = 92) and CA1 pyramidal cells (n = 40). Pharmacologic analysis of VDCC, on heterotopic, normotopic, and CA1 pyramidal cells, revealed an similar to70% blockade of peak Ca2+ current with nifedipine and amiloride (L- and T-type channel blockers, respectively). Inhibition of VDCC, for all three cell types, also was similar when more specific Ca2+ channel antagonists were used [e.g., omega-**conotoxin** GVIA (N-type), omega-agatoxin KT (P/Q-type), and sFTX-3.3 (P-type)]. VDCC modulation by norepinephrine (NE) or **adrenergic receptor**-specific agonists [clonidine (alpha(2)), isoproterenol (beta), and phenylephrine (**alpha**(1))] was similar for heterotopic and CA1 pyramidal cells.

Conclusions: Heterotopic neurons do not appear to exhibit Ca2+ channel abnormalities that could contribute to the reported hyperexcitability associated with MAM-exposed rats.

L66 ANSWER 3 OF 32 EMBASE

on STN DUPLICATE 1

ACCESSION NUMBER: 2003398668 EMBASE
TITLE: Adrenergic regulation of the intracellular [Ca(2+)] and voltage-operated Ca(2+) channel currents in the rat prostate neuroendocrine cells.
AUTHOR: Kim J.H.; Shin S.Y.; Nam J.H.; Hong E.-K.; Chung Y.-S.; Jeong J.Y.; Kang J.; Uhm D.-Y.; Kim S.J.
CORPORATE SOURCE: S.J. Kim, Department of Physiology, Sungkyunkwan Univ. Sch. of Medicine, Suwon 440-746, Korea, Republic of. sjoonkim@med.skku.ac.kr
SOURCE: Prostate, (1 Oct 2003) 57/2 (99-110).
Refs: 31
ISSN: 0270-4137 CODEN: PRSTDS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
003 Endocrinology
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB BACKGROUND. The prostate gland contains numerous neuroendocrine cells (PNECs) innervated by adrenergic neurons. PNECs are believed to influence the growth and physiological function of the prostate gland via paracrine release of hormones. MATERIALS AND METHODS. Using fura-2 fluorescence measurement and patch-clamp techniques, we investigated the effects of adrenergic stimulation on cytosolic concentration of Ca(2+) ([Ca(2+)](c)) and high voltage-activated Ca(2+) channel currents (HVA-I (Ca)) of the putative rat prostate neuroendocrine cells (RPNECs) freshly isolated by an enzymic digestion. RESULTS. Noradrenaline (NA, 1 μM) induced a sharp, transient increase of [Ca(2+)](c) measured by the fura-2 fluorescence. Pharmacological studies showed that .**alpha**.**1**-**adrenoceptors** (.**alpha**.**1**-ARs) coupled with PLC/IP(3) signaling pathway induce the release of stored Ca(2+), which subsequently recruits store-operated Ca(2+) entry pathways. In the whole-cell voltage clamp experiment, NA decreased the amplitude of HVA-I(Ca) by 40%, which was mimicked by an α2-AR agonist (UK14304) but not by an .**alpha**.**1**-AR agonist (phenyleprine). After selective blockade of N-type Ca (2+) channels by ω-**conotoxin** GVIA, the addition of NA showed no further inhibition on the remaining L-type Ca(2+) channel currents. The adrenergic inhibition of HVA-I(Ca) was partially prevented by the pretreatment with pertussis toxin (PTX) (5 pg/ml, 4 hr, 37°C). CONCLUSIONS. RPNECs express both .**alpha**.**1**- and α2-ARs, signaling the release of stored Ca(2+) and the inhibition of N-type Ca(2+) channels, respectively. .COPYRGT. 2003 Wiley-Liss, Inc.

L66 ANSWER 4 OF 32 MEDLINE on STN
ACCESSION NUMBER: 2002268445 MEDLINE
DOCUMENT NUMBER: 22004225 PubMed ID: 12007990
TITLE: Toxins 'R' Us: more pharmacological tools from nature's superstore.
AUTHOR: Harvey Alan L
CORPORATE SOURCE: Dept of Physiology and Pharmacology, and Strathclyde Institute for Drug Research, University of Strathclyde, 27 Taylor Street, Glasgow, UK G4 0NR.. a.l.harvey@strath.ac.uk
SOURCE: TRENDS IN PHARMACOLOGICAL SCIENCES, (2002 May) 23 (5) 201-3.
Journal code: 7906158. ISSN: 0165-6147.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020515
Last Updated on STN: 20020830
Entered Medline: 20020829

AB Conus venoms from marine cone snails continue to provide novel bioactive components. Two new classes of **conopeptide** specifically block **alpha(1)-adrenoceptors** (rho-**conopeptide**) and noradrenaline transporters (chi-**conopeptides**). Both classes are small peptides with two disulfide bonds. Rho-conopeptide is structurally similar to alpha-conotoxins, which block nicotinic acetylcholine receptors, whereas the chi-conopeptides are unrelated to other conotoxins. Both types of conopeptides are non-competitive blockers. Because these peptides demonstrate greater selectivity than current drugs in clinical use, they could lead to the development of improved therapeutics.

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ACCESSION NUMBER: 2003:50787 BIOSIS
DOCUMENT NUMBER: PREV200300050787
TITLE: Toxins 'R' Us: More pharmacological tools from nature's superstore.
AUTHOR(S): Harvey, Alan L. [Reprint Author]
CORPORATE SOURCE: Dept of Physiology and Pharmacology, Strathclyde Institute for Drug Research, University of Strathclyde, 27 Taylor Street, Glasgow, G4 0NR, UK
a.l.harvey@strath.ac.uk
SOURCE: Trends in Pharmacological Sciences, (May 2002) Vol. 23, No. 5, pp. 201-203. print.
ISSN: 0165-6147 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jan 2003
Last Updated on STN: 22 Jan 2003

AB Conus venoms from marine cone snails continue to provide novel bioactive components. Two new classes of conopeptide specifically block alpha1-adrenoceptors (rho-conopeptide) and noradrenaline transporters (chi-conopeptides). Both classes are small peptides with two disulfide bonds. rho-Conopeptide is structurally similar to alpha-conotoxins, which block nicotinic acetylcholine receptors, whereas the chi-conopeptides are unrelated to other conotoxins. Both types of conopeptides are non-competitive blockers. Because these peptides demonstrate greater selectivity than current drugs in clinical use, they could lead to the development of improved therapeutics.

L66 ANSWER 6 OF 32 AQUASCI COPYRIGHT (C) 2004 FAO (on behalf of the ASFA Advisory Board). All Rights Reserved. on STN DUPLICATE 3

ACCESSION NUMBER: 2002:79944 AQUASCI
DOCUMENT NUMBER: ASFA3 2002
TITLE: Two new classes of **conopeptides** inhibit the **alpha 1-adrenoceptor** and noradrenaline transporter
AUTHOR: Sharpe, I.A.; Gehrmann, J.; Loughnan, M.L.; Thomas, L.; Adams, D.A.; Atkins, A.; Palant, E.; Craik, D.J.; Adams, D.J.; Alewood, P.F.; Lewis, R.J.*
CORPORATE SOURCE: Institute for Molecular Bioscience, University of Queensland, Brisbane 4072, Australia); E-mail: r.lewis@imb.uq.edu.a
SOURCE: Nature Neuroscience [Nat. Neurosci.], (20010900) vol. 4, no. 9, pp. 902-907.
ISSN: 1097-6256.
DOCUMENT TYPE: Journal
FILE SEGMENT: ASFA3
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cone snails use venom containing a cocktail of peptides ('**conopeptides**') to capture their prey. Many of these peptides also target mammalian receptors, often with exquisite selectivity. Here we report the discovery of two new classes of **conopeptides**. One

class targets **alpha 1-adrenoceptors** (rho -TIA from the fish-hunting Conus tulipa), and the second class targets the neuronal noradrenaline transporter (chi -MrIA and chi -MrIB from the mollusk-hunting C. marmoreus). rho -TIA and chi -MrIA selectively modulate these important membrane-bound proteins. Both peptides act as reversible non-competitive inhibitors and provide alternative avenues for the identification of inhibitor drugs.

L66 ANSWER 7 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2000:241268 CAPLUS
DOCUMENT NUMBER: 132:288791
TITLE: ρ- **Conotoxin** peptides with .**alpha** .**1-adrenoceptor** antagonist activity, nucleic acids encoding them, antibodies, and therapeutic uses
INVENTOR(S): Lewis, Richard James; Alewood, Paul Francis; Sharpe, Iain Andrew
PATENT ASSIGNEE(S): The University of Queensland, Australia
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020443	A1	20000413	WO 1999-AU843	19991001
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2344551	AA	20000413	CA 1999-2344551	19991001
AU 9963211	A1	20000426	AU 1999-63211	19991001
AU 767850	B2	20031127		
EP 1117681	A1	20010725	EP 1999-950405	19991001
EP 1117681	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526097	T2	20020820	JP 2000-574554	19991001
AT 238346	E	20030515	AT 1999-950405	19991001

PRIORITY APPLN. INFO.:
AU 1998-6273 A 19981002
AU 1998-9862 A 19981002
WO 1999-AU843 W 19991001

AB The invention provides an isolated, synthetic or recombinant ρ-**conotoxin** peptide having selective .**alpha**.**1**-**adrenoceptor** antagonist activity, nucleic acid mols. encoding all or part of such peptides, antibodies to such peptides, and uses and methods of treatment involving them. The peptides may be used in the treatment of urinary or cardiovascular conditions, mood disorders, pain, or inflammation.

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ACCESSION NUMBER: 2000063944 EMBASE
TITLE: Postural hypotension following N-type Ca2+ channel blockade is amplified in experimental hypertension.
AUTHOR: Wright C.E.; Hawkes A.L.; Angus J.A.
CORPORATE SOURCE: C.E. Wright. c.wright@pharmacology.unimelb.edu.au

SOURCE: Journal of Hypertension, (2000) 18/1 (65-73).
Refs: 36
ISSN: 0263-6352 CODEN: JOHYD3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective. To determine the relative importance of the cardiac and vascular sympathetic components of the orthostatic response to 90°head-up tilt after N-type calcium-channel blockade in normotensive (sham renal cellophane wrap) and hypertensive (renal wrap) conscious rabbits. Methods. The effects of N-type calcium-channel blockade with ω- **conotoxin** GVIA (ω-CTX, 10 μg/kg i.v. bolus) were assessed in the absence or presence of cardiac block by propranolol and methscopolamine. These were contrasted with the effects of .**alpha**.1-**adrenoceptor** antagonism (prazosin 0.5 mg/kg i.v. bolus, in the presence of cardiac block) or ganglion blockade (mecamylamine 4 mg/kg i.v. bolus). Results. In vehicle (0.9% saline) treatment groups, the response to tilt consisted of a small presser effect (4 ± 2 and 7 ± 1 mmHg) and tachycardia (29 ± 6 and 17 ± 6 beats/min) in sham (n = 6) and wrap (n = 5) rabbits, respectively. After prazosin administration (with cardiac block), there were significant falls in MAP of 3 ± 1 and 7 ± 2 mmHg in sham (n = 7) and wrap (n = 6) rabbits, respectively, in response to tilt. ω-CTX caused postural hypotensive responses of 8 ± 2 and 13 ± 2 mmHg in sham (n = 6) and wrap (n = 7) rabbits, respectively, and 7 ± 1 and 14 ± 2 mmHg in sham (n = 7) and wrap (n = 7) rabbits with prior cardiac block. Similarly, mecamylamine caused falls in MAP of 8 ± 1 and 10 ± 2 mmHg in response to tilt in sham (n = 6) and wrap (n = 9) animals, respectively. Conclusion. Sympathetic vasoconstrictor effecters are primarily responsible for maintaining blood pressure during tilt in conscious rabbits. The postural hypotension caused by sympatholytic agents is about double in hypertensive rabbits, and N-type calcium-channel blockade is as effective as ganglion blockade at inducing this syndrome. (C) Lippincott Williams and Wilkins.

L66 ANSWER 9 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2001:80634 CAPLUS
DOCUMENT NUMBER: 134:126377
TITLE: Differential effects of ω-conotoxin GVIA, tetrodotoxin and prolonged cold storage on purinergic and adrenergic transmission in isolated canine splenic artery
AUTHOR(S): Yang, Xiao-Ping; Chiba, Shigetoshi
CORPORATE SOURCE: Department of Pharmacology, Shinshu University School of Medicine, Matsumoto, 390-8621, Japan
SOURCE: Journal of Cardiovascular Pharmacology (2000), 36(6, Suppl. 2), S5-S8
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Double-peaked vasoconstrictions (biphases of vasoconstrictions) were readily induced in the conditions of 30 s trains of pulses at 1 Hz in the isolated, perfused canine splenic artery. P2X purinoceptors have previously been shown to be involved mainly in the first-peaked response and α1-adrenoceptors mostly in the second. The treatment with 10 nM ω-conotoxin GVIA (ω-CTX) produced a parallel inhibitory effect on the first- and second-peaked vasoconstrictor responses to nerve stimulation. A submaximal concentration of tetrodotoxin (TTX) (3 nM) did not affect the first peak of constriction, but strongly inhibited the second peak, although a larger dose of TTX (30 nM) abolished either the first- or

second-peaked response. On the other hand, after cold storage at 4°C for 7 days, the first-peaked vasoconstriction markedly decreased, whereas the second-peaked response was not significantly modified. In conclusion: (1) ω-CTX-sensitive calcium channels may produce a parallel modulation of purinergic and adrenergic components of sympathetic cotransmission; (2) TTX-sensitive sodium channels may have a more important role in controlling the adrenergic rather than purinergic transmission; and (3) the function of purinergic transmission of sympathetic nerve might be affected more strongly than that of adrenergic transmission in the cold-stored canine splenic artery.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L66 ANSWER 10 OF 32 EMBASE
on STN DUPLICATE 7

ACCESSION NUMBER: 1999200394 EMBASE
TITLE: Norepinephrine inhibits a toxin resistant Ca2+ current in carotid body glomus cells: Evidence for a direct G protein mechanism.
AUTHOR: Overholt J.L.; Prabhakar N.R.
CORPORATE SOURCE: J.L. Overholt, Dept. of Physiology and Biophysics, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, OH 44106-4970, United States
SOURCE: Journal of Neurophysiology, (1999) 81/1 (225-233).
Refs: 34
ISSN: 0022-3077 CODEN: JONEA4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Previous studies have demonstrated that endogenous norepinephrine (NE) inhibits carotid body (CB) sensory discharge, and the cellular actions of NE have been associated with inhibition of Ca2+ current in glomus cells. The purpose of the present study was to elucidate the characteristics and mechanism of NE inhibition of whole cell Ca2+ current isolated from rabbit CB glomus cells and to determine the type(s) of Ca2+ channel involved. NE (10 μM) inhibited 24 ± 2% (SE) of the macroscopic Ca2+ current measured at the end of a 25 ms pulse to 0 mV and slowed activation of the current. The α2 **adrenergic receptor** antagonist, SK and F 86466, attenuated these effects. Inhibition by NE was fast and voltage-dependent i.e., maximal at - 10 mV and then diminished with stronger depolarizations. This is characteristic of G protein βγ subunit interaction with the . **alpha.1** subunit of certain Ca2+ channels, which can be relieved by depolarizing steps. A depolarizing step (30 ms to +80 mV) significantly increased (14 + 1%) current in the presence of NE, whereas it had no effect before application of NE (1 ± 1%). To further test for the involvement of G proteins, NE was applied to cells where intracellular GTP was replaced by GDP-βS. NE had little or no effect on Ca2+ current in cells dialyzed with GDP-βS. To determine whether NE was inhibiting N- and/or P/Q-type channels, we applied NE in the presence of ω-**conotoxin** MVIIC (MVIIC). In the presence of 2.5 μM MVIIC, NE was equally potent at inhibiting the Ca2+ current (23 ± 4% vs. 23 ± 4% in control), suggesting that NE was not exclusively inhibiting N- or P/Q-type channels. NE was also equally potent (30 ± 2% vs. 26 ± 4% in control) at inhibiting the Ca2+ current in the presence of 2 μM nisoldipine, suggesting that NE was not inhibiting L-type channels. Further, NE inhibited a significantly larger proportion (47 ± 6%) of the resistant Ca2+ current remaining in the presence of NISO and MVIIC. These results suggest that NE inhibition of Ca2+ current in rabbit CB glomus cells is mediated in most part by effects on the resistant, non L-, N-, or P/Q-type channel and involves a direct G protein βγ interaction with this channel.

L66 ANSWER 11 OF 32 EMBASE

on STN DUPLICATE 8
ACCESSION NUMBER: 1999401737 EMBASE
TITLE: Two-phase responses of acid expulsion triggered by alpha-1a adrenoceptor in CHO cell.
AUTHOR: Taniguchi T.; Inagaki R.; Takauji R.; Suzuki F.; Muramatsu I.
CORPORATE SOURCE: T. Taniguchi, Department of Pharmacology, School of Medicine, Fukui Medical University, 23 Shimoaizuki, Matsuoka, Fukui 910-1193, Japan
SOURCE: Folia Pharmacologica Japonica, (1999) 114/SUPPL. 1 (110P-112P).
Refs: 2
ISSN: 0015-5691 CODEN: NYKZAU
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB Using microphysiometer, we have investigated acid expulsion from CHO cells expressing human alpha-1a **adrenoceptor**. Time course of extracellular acidification rate after noradrenaline stimulation had two phases; one with a peak within 10 s reached several folds of base rate, and another increased gradually to two folds of base rate and reached plateau around two min. Both phases showed concentration-dependent increase of acidification rates in response to noradrenaline but had distinct pEC50 values; 6.0 for rapid phase and 6.6 for late phase. Amiloride and its analogs inhibited both phases entirely, suggesting that Na/H exchanger mainly mediated these acid expulsion responses. Elimination of Ca by BAPTA/EGTA treatment resulted in extensive reductions of the rapid phase response but small decrease of the late phase response. Several Ca channel blockers, Ni and LOE908 also suppressed the rapid phase while nifedipine, verapamil, SKF96365 and ω- **conotoxin** GIVA did not. Repeated stimulation with noradrenaline enhanced inhibitory effect of blockers. These results indicate that Ca is one of the elements in the rapid phase but not in the late phase of acid expulsion from CHO cells in response to **alpha-1 adrenoceptor** stimulation and suggest that Ca from both intracellular storage and some type of Ca channel dominantly participates in the rapid phase.

L66 ANSWER 12 OF 32 EMBASE
on STN DUPLICATE 9
ACCESSION NUMBER: 97345911 EMBASE
DOCUMENT NUMBER: 1997345911
TITLE: Activation of α2-adrenoceptors causes inhibition of calcium channels but does not modulate inwardly-rectifying K+ channels in caudal raphe neurons.
AUTHOR: Li Y.-W.; Bayliss D.A.
CORPORATE SOURCE: D.A. Bayliss, Department of Pharmacology, University of Virginia, Charlottesville, VA 22908, United States
SOURCE: Neuroscience, (1998) 82/3 (753-765).
Refs: 38
ISSN: 0306-4522 CODEN: NRSCDN
PUBLISHER IDENT.: S 0306-4522(97)00312-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Many neurotransmitter receptors that interact with pertussis toxin-sensitive G proteins, including the α2- **adrenergic receptor**, can modulate both voltage-dependent calcium channels and G protein-coupled inwardly- rectifying K+ channels. Serotonergic neurons of the medulla oblongata (nucleus raphe obscurus and nucleus raphe pallidus), which provide a major projection to sympathetic and motor

output systems, receive a catecholaminergic input and express α2- **adrenergic receptors**. Therefore, we tested the effects of norepinephrine on voltage-dependent calcium channels and G protein-coupled inwardly-rectifying K+ channels in neonatal raphe neurons using whole-cell recording in a brainstem slice preparation. Calcium channel currents were inhibited by norepinephrine in the majority of raphe neurons tested (88%) and in all identified tryptophan hydroxylase-immunoreactive (i.e. serotonergic) neurons. When tested in the same neurons, the magnitude of calcium current inhibition by norepinephrine (.apprx.25%) was less than that induced by 5-hydroxytryptamine (.apprx.50%). The norepinephrine- induced calcium current inhibition was mediated by α2- **adrenergic receptors**; it was mimicked by UK 14304, an α2- **adrenergic receptor** agonist and blocked by idazoxan, an α2- **adrenergic receptor** antagonist, but not affected by prazosin or propanolol (. **alpha**.1 and β adrenergic antagonists, respectively). Calcium current inhibition by norepinephrine was essentially eliminated following application of ω- **Conotoxin** GVIA and to-Agatoxin IVA, indicating that norepinephrine modulated N- and P/Q-type calcium channels predominantly. Calcium current inhibition by norepinephrine was voltage-dependent and mediated by pertussis toxin-sensitive G proteins. Thus, as expected, α2- **adrenergic receptor** activation inhibited N- and P/Q-type calcium currents in medullary raphe neurons via pertussis toxin-sensitive G proteins. In parallel experiments, however, we found that norepinephrine had no effect on G protein-coupled inwardly-rectifying K+ channels in any raphe neurons tested, despite the robust activation of those channels in the same neurons by 5- hydroxytryptamine. Together, these data indicate that α2- **adrenergic receptors** can modulate N- and P/Q-type calcium channels in caudal medullary raphe neurons but do not couple to the G protein-coupled inwardly-rectifying K+ channels which are also present in those cells. This is in contrast to the effect of 5-hydroxytryptamine(1A) receptor activation in caudal raphe neurons, and indicates a degree of specificity in the signalling by different pertussis toxin-sensitive G protein-coupled receptors to voltage-dependent calcium channels and G protein-coupled inwardly-rectifying K+ channels even within the same cell system.

L66 ANSWER 13 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 10

ACCESSION NUMBER: 1998067020 EMBASE
TITLE: Voltage-dependent calcium currents in bulbospinal neurons of neonatal rat rostral ventrolateral medulla: Modulation by α2-adrenergic receptors.
AUTHOR: Li Y.-W.; Guyenet P.G.; Bayliss D.A.
CORPORATE SOURCE: D.A. Bayliss, Dept. of Pharmacology, University of Virginia, 5017 Jordan Hall, Charlottesville, VA 22908, United States
SOURCE: Journal of Neurophysiology, (1998) 79/2 (583-594). Refs: 47
ISSN: 0022-3077 CODEN: JONEA4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The properties and modulation by norepinephrine (NE) of voltage- dependent calcium currents were studied in bulbospinal neurons (n = 116) of the rostral ventrolateral medulla (RVLM) using whole cell patch-clamp techniques in neonatal rat brain stem slices. RVLM bulbospinal neurons were identified visually by their location in slices and by the presence of flourescein isothiocyanate-tagged microbeads, which were injected into the spinal cord before the experiment; RVLM neurons were filled with Lucifer yellow during recordings, and the slice was processed for

detection of tyrosine hydroxylase immunoreactivity (TH-IR). Thirty-four of 42 recovered cells (81%) were positive for TH-IR, indicating that most recorded cells were C1 neurons. Bulbospinal RVLM neurons expressed a prominent high-voltage- activated (HVA) calcium current, which began to activate at -30 to -40 mV (from a holding potential of -60 or -70 mV), and peaked at .apprx.0 mV (0.8 ± 0.1 nA; mean ± SE). HVA current comprised predominantly ω- **conotoxin** GVIA- sensitive, N-type and ω-agatoxin IVA-sensitive, P/Q-type components, with smaller dihydropyridine-sensitive, L-type, and residual current components. Most RVLM bulbospinal neurons (n = 44/52, including 12/14 histologically identified C1 cells) also expressed low-voltage-activated (LVA) calcium current. LVA current began to activate at .apprx.-60 mV (from a holding potential of -100 mV) and was nearly completely inactivated at -50 mV with a half- inactivation potential of -70 ± 2 mV. The amplitude of LVA current at -50 mV was 78 ± 24 pA with Ba2+ and 156 ± 38 pA with Ca2+ as a charge carrier. NE inhibited HVA current in most bulbospinal RVLM neurons (n = 70/77) with an EC50 of 1.2 μM; NE had no effect on LVA current. Calcium current inhibition by NE was mediated by α2- **adrenergic receptors** (α2-ARs) as the effect was mimicked by the selective α2-AR agonist, UK-14,304, and blocked by idazoxan, an α2-AR antagonist, but unaffected by prazosin and propranolol (.**alpha.1**- and β-AR antagonists, respectively). Most of the NE- sensitive calcium current was N- and P/Q-type. NE-induced inhibition of calcium current evoked by action potential waveforms (APWs) was significantly larger than that evoked by depolarizing steps (34 ± 2.5 vs. 23 ± 2.7%; P < 0.05). Although inhibition of calcium current was voltage dependent and partially relieved by strong depolarizations, when calcium currents were evoked with a 10-Hz train of APWs as a voltage command, the inhibitory effect of NE was maintained throughout the train. In conclusion, bulbospinal RVLM neurons, including C1 cells, express multiple types of calcium currents. Inhibition of HVA calcium current by NE may modulate input-output relationships and release of transmitters from C1 cells.

L66 ANSWER 14 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:473549 BIOSIS
DOCUMENT NUMBER: PREV199799772752
TITLE: Identification of two novel **conotoxin** targets: Uptake-1 and the **alpha-1-adrenoceptor**.
AUTHOR(S): Sharpe, L. A. [Reprint author]; Lewis, R. J. [Reprint author]; Gehrmann, J. [Reprint author]; Alewood, P. F. [Reprint author]; Adams, D. J.
CORPORATE SOURCE: Centre Drug Design Dev., Univ. Queensland, St. Lucia, QLD 4072, Australia
SOURCE: Journal of the Autonomic Nervous System, (1997) Vol. 65, No. 2-3, pp. 149.
Meeting Info.: Inaugural Conference of the International Society for Autonomic Neuroscience. Cairns, Queensland, Australia. September 14-19, 1997.
CODEN: JASYDS. ISSN: 0165-1838.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Nov 1997
Last Updated on STN: 4 Nov 1997

L66 ANSWER 15 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 11
ACCESSION NUMBER: 1995:544514 BIOSIS
DOCUMENT NUMBER: PREV199698558814
TITLE: Omega-conotoxin GVIA and prazosin, but not felodipine, cause postural hypotension in rabbits.
AUTHOR(S): Hawkes, Anna L.; Angus, James A.; Wright, Christine E.

[Reprint author]
CORPORATE SOURCE: Dep. Pharmacol., Univ. Melbourne, Grattan Street, Parkville, VIC 3052, Australia
SOURCE: Clinical and Experimental Pharmacology and Physiology, (1995) Vol. 22, No. 10, pp. 711-716.
ISSN: 0305-1870.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Dec 1995
Last Updated on STN: 31 Dec 1995

AB 1. The aim was to compare the effect of N-type calcium channel blockade by omega-**conotoxin** GVIA (omega-CTX) with **alpha**-**1-adrenoceptor** or L-type calcium channel blockade on postural adaptation in conscious rabbits. 2. Orthostatic responses were assessed by rapidly tilting the rabbits through 90 degree for 1 min. Tilts were performed before, 30 and 60 min after i.v. bolus administration of vehicle (propylene glycol 0.17mL/kg; n = 8), prazosin (0.5 mg/kg; n = 8), felodipine (30 mu-g/kg; n = 8) or omega-CTX (3 and 7 mu-g/kg; n = 9). 3. Prazosin, felodipine or omega-CTX caused significant falls in mean arterial pressure (MAP) with corresponding increases in heart rate (HR). Vehicle administration had no effect on MAP but caused a small fall in HR. 4. Before drug or vehicle administration, a small rise in MAP and HR occurred in response to tilt in all rabbits. In the vehicle treatment group, similar responses were observed to tilt at 30 and 60 min. Postural hypotension was observed in the prazosin treatment group, but not following administration of felodipine. Tilts 30 and 60 min after omega-CTX (3 mu-g/kg) caused an increase in HR but no change in MAP, different to the small pressor response observed following vehicle administration. However, following administration of omega-CTX 7 mu-g/kg (total dose, 10 mu-g/kg), significant falls in MAP with tachycardia were observed in response to tilt. 5. In conclusion, orthostatic hypotension was observed following acute alpha-1-adrenoceptor or N-type calcium channel blockade in the conscious rabbit. These findings are compatible with the expectation that agents which are directly sympatholytic interfere with postural adaptation. In contrast, L-type calcium channel antagonism with felodipine did not elicit postural hypotension.

L66 ANSWER 16 OF 32 EMBASE
on STN
ACCESSION NUMBER: 95372973 EMBASE
DOCUMENT NUMBER: 1995372973
TITLE: Effects of the putative P-type calcium channel blocker, R,R-(-)-daurisoline on neurotransmitter release.
AUTHOR: Waldmeier P.C.; Wicki P.; Frostl W.; Bittiger H.; Feldtrauer J.-J.; Baumann P.A.
CORPORATE SOURCE: Research Department, Pharmaceuticals Division, K-125.607, Ciba-Geigy Ltd.,CH-4002 Basel, Switzerland
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (1995) 352/6 (670-678).
ISSN: 0028-1298 CODEN: NSAPCC
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
008 Neurology and Neurosurgery
023 Nuclear Medicine
052 Toxicology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The alkaloid and medicinal herb constituent, R,R-(-)-daurisoline, was originally reported to be a N-type Ca2+ channel blocker, but newer evidence indicates that it is a blocker of P-type Ca2+ channels. To clarify its specificity with respect to N- and P-channels, we compared its effects on the electrically induced release of endogenous glutamate, 3H-GABA and 3H-noradrenaline, from brain slices with those of

ω-agatoxin IVA and ω- **conotoxin** GVIA. Like ω-agatoxin IVA (but with about 1000-fold lower potency), and unlike ω- **conotoxin** GVIA, R,R-(-)-daurisoline inhibited the release of 3H-GABA and glutamate, with IC50 values of 8 and 18 μM. However, inhibition particularly of 3H-GABA release was more complete than by ω-agatoxin IVA, indicating interaction with one or more additional voltage-sensitive Ca2+ channels, possibly the Q-type. Its potency to inhibit glutamate release elicited either electrically, by veratrine or by high concentrations of K+ was similar, in contrast to sodium channel blockers. The effects of R,R-(-)-daurisoline on the release of 3H-noradrenaline, 3H-dopamine and 3H-acetylcholine were in agreement with previous knowledge from experiments with ω-agatoxin IVA suggesting an involvement of P-channels. A weak inhibition of 3H-noradrenaline release at 10 μM, similar to that by ω-agatoxin IVA at 0.03 μM, was occluded by α2-antagonistic properties and could be unmasked in presence of rauwolscine. At 10 μM, it also inhibited electrically evoked 3H-dopamine and 3H-5-hydroxytryptamine release and caused a marked spontaneous release of all three monoamines in a reserpine-like manner. Spontaneous and evoked release of 3H-acetylcholine was inhibited by about 25% at 10 μM. In radioligand binding studies, R,R-(-)-daurisoline interacted with **.alpha.** **1**- and α2- **adrenoceptors**, 5-HT2 and muscarinic cholinergic receptors with IC50 values close to 1 μM, and with μ opiate receptors even with 0.18 μM. Atropine reduced the weak inhibitory effect of R,R-(-)-daurisoline on 3H-acetylcholine release somewhat, suggesting that it was brought about by both P channel blockade and cholinergic agonist activity. The effect on 3H-GABA release was unaffected by naloxone, indicating that the interaction of R,R-(-)-daurisoline with μ opiate receptors is antagonistic. The pattern of effects on neurotransmitter release observed with R,R-(-)-daurisoline resembles that of ω-agatoxin IVA and supports previous electrophysiological data suggesting that the compound blocks P-type voltage-sensitive Ca2+ channels. However, the more complete blockade of amino acid release by R,R-(-)-daurisoline suggests interaction with additional Ca2+ channel subtypes. Although it does also possess other pharmacological properties, we think that the compound is suitable to test whether blockade of glutamate release via voltage-sensitive Ca2+ channels is a viable concept to obtain novel neuroprotective and/or anticonvulsant compounds.

L66 ANSWER 17 OF 32 JICST-EPlus COPYRIGHT 2004 JST on STN
ACCESSION NUMBER: 960175661 JICST-EPlus
TITLE: Changes in Calcium Channels of Cerebral Cortex Following the Development of Tolerance to Morphine.
AUTHOR: SUEMATSU MOTOO
CORPORATE SOURCE: Osaka Univ., Fac. of Dent.
SOURCE: Osaka Daigaku Shigaku Zasshi (Journal of Osaka University Dental Society), (1995) vol. 40, no. 1, pp. 211-225. Journal Code: G0883A (Fig. 12, Tbl. 1, Ref. 61) CODEN: ODSZA2; ISSN: 0473-4629
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB Although potent analgesic action of morphine makes it useful in relieving cancer pain, its use is limited owing to the feature inducing tolerance. It is now accepted that opioids inhibit the influx of Ca2+ thereby reducing the release of transmitters which might result in analgesic effect. Thus, evidences have been also accumulated that voltage-dependent Ca2+ channels(VDCC) may be involved in the process of the development of tolerance. This is supported by the finding that clonidine reducing Ca2+ influx through the activation of A2- **adrenoceptors** attenuates a withdrawal response for morphine dependence. In the present study, change in Ca2+ dynamics following morphine or clonidine treatments were determined by measuring high K+-induced 45Ca uptake into synaptosomes, Ca2+ antagonist bindings to membrane fractions and in vivo

analgesic effect of Ca2+ antagonists with the special interest determining the subtype of VDCC. The followings were observed. 1) Prolonged administration of morphine and clonidine in mice developed cross-tolerance in analgesic test. In the test, Ω- **conotoxin** GVIA(GVIA), an N-type VDCC antagonist, -induced analgesia was reduced in both tolerant groups while nifedipine, a L-type VDCC antagonist, -induced analgesia was reduced only in clonidine treated group. 2) High K+-induced 45Ca uptake into synaptosomes increased in the fractions prepared from both morphine and clonidine tolerant groups. 3) In VDCC antagonist binding experiments, 3H-PN 200-110, a L-type VDCC antagonist, binding increased in morphine tolerant group while decreased in clonidine treated group. An increase of 125I-GVIA binding was observed in both morphine and clonidine tolerant groups. In all cases, there was no change in the binding affinity. 4) Photoaffinity labeling experiments employing 125I-GVIA revealed incorporation of activity into 230-300kDa proteins corresponding to . **ALPHA.1** subunit of N-type VDCC. (author abst.)

L66 ANSWER 18 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 12
ACCESSION NUMBER: 94153959 EMBASE
DOCUMENT NUMBER: 1994153959
TITLE: Dopamine inhibits a sustained calcium current through activation of alpha adrenergic receptors and a GTP-binding protein in adult rat sympathetic neurons.
AUTHOR: Aguayo L.G.; Grossie J.
CORPORATE SOURCE: Institute of Chemistry, Catholic University, Avenida Brasil 2950,Valparaiso, Chile
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1994) 269/2 (503-508).
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although it is suspected that dopamine (DA) inhibits a Ca++ current in sympathetic neurons, the receptor and the Ca++ channel type involved are still unknown. We found that DA caused a reversible inhibition on ω-**conotoxin** sensitive and resistant Ca++ currents in the superior cervical ganglion (SCG). The concentration of DA that induced half-maximal inhibition was 3.0 μM. The DA receptor agonists (±)-SKF-38393 (D1 type) and quinpirole (D2 type) appeared unable to induce an inhibition of the Ca++ current. Furthermore, the receptor antagonists SCH-23390 (D1 type) and (-)- sulpiride (D2 type) did not prevent the inhibitory effect of DA. This suggests that the effect of DA on the Ca++ current was not due to activation of DA receptors. The inhibition of the Ca++ current by DA was reduced by application of 1 μM phentolamine, a nonselective alpha adrenergic antagonist, and by prazosin and yohimbine, **alpha-1** and alpha-2 receptor antagonists, respectively. The beta **adrenergic receptor** antagonist propranolol did not block the effect of DA. A guanine nucleotide-binding protein appears to be involved in the activation of **adrenergic receptors** by DA. The addition of GTP-γ-S (0.1 mM) to the intracellular solution produced an effect similar to that of DA. Incubation of sympathetic neurons with pertussis toxin reduced the effect of DA by 90%. The results indicate that DA reduces the number of available Ca++ channels in sympathetic neurons by activation of alpha **adrenergic receptors**, which are associated with a pertussis-sensitive GTP-binding protein.

L66 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 13
ACCESSION NUMBER: 1994:596535 CAPLUS
DOCUMENT NUMBER: 121:196535
TITLE: α1-Adrenoceptors in rat dorsal raphe neurons: regulation of two potassium conductances

AUTHOR(S): Pan, Z. Z.; Grudt, T. J.; Williams, J. T.
CORPORATE SOURCE: Vollum Inst., Oregon Health Sci. Univ., Portland, OR, 97201, USA
SOURCE: Journal of Physiology (Cambridge, United Kingdom) (1994), 478(3), 437-47
CODEN: JPHYA7; ISSN: 0022-3751
DOCUMENT TYPE: Journal
LANGUAGE: English

AB α1-Adrenoceptor activation caused two sep. effects in rat dorsal raphe neurons: a depolarization and an increase in the duration of the after-hyperpolarization following the action potential. The depolarization often results in repetitive action potentials. The α1-adrenoceptor antagonists prazosin and WB 4101 blocked the depolarization induced by phenylephrine. The concentration-response curve to phenylephrine was shifted to the right by WB 4101. Under voltage clamp, α1-adrenoceptor agonists caused an inward current at -60 mV, which often became smaller at neg. potentials but rarely reversed polarity even at strongly neg. potentials. Using whole-cell recording, the inward current reversed polarity at the equilibrium potential for potassium in the majority of cells. Intracellular Cs+ decreased or abolished the α1-mediated inward current. The inward current was dependent on external calcium, but not on the degree of internal calcium buffering. Removal of external calcium or addition of MgCl2, CoCl2 or CdCl2 reduced or blocked the effects of α1-adrenoceptor agonists. Barium and strontium supported and even augmented the inward current induced by . **alpha.1-adrenoceptor** agonists, whereas nifedipine and ω- **conotoxin** had no effect. In contrast, internal dialysis with the calcium chelator BAPTA did not inhibit the inward current. The α1-induced depolarization was blocked (or occluded) by the inclusion of GTP-γ-S (100 μM) in the recording pipet. The phorbol-ester 4-phorbol 12,13-dibutyrate (PDBu) had no action on the membrane potential and depressed the phenylephrine-induced depolarization. This depression was reversed by the non-selective protein kinase inhibitor staurosporin. Phenylephrine and noradrenaline increased a late component of the after-hyperpolarization (late-AHP) that followed a single action potential. The α1-sensitive late-AHP was blocked by apamin, suggesting that it is a calcium-dependent potassium conductance. Thapsigargin reduced the duration of the late-AHP and blocked the phenylephrine-mediated prolongation. Caffeine also augmented the late-AHP and ryanodine blocked the augmentation induced by caffeine. The augmentation induced by phenylephrine was not occluded by caffeine and was still present after the caffeine-induced augmentation was blocked by ryanodine. In slices pretreated with manoalide the depolarization induced by α1-agonists was not changed; however, the late-AHP was reduced in duration and the α1-receptor-mediated augmentation of the late-AHP was decreased. The results suggest that the depolarization of dorsal raphe neurons by α1-adrenoceptor activation is through a decrease in potassium conductance that is independent of the activation of the phospholipase C pathway. The augmentation of the late-AHP is mediated by release of calcium from intracellular stores and may serve to regulate activity during the depolarization induced by α1-adrenoceptor activation.

L66 ANSWER 20 OF 32 DISSABS COPYRIGHT (C) 2004 ProQuest Information and Learning Company; All Rights Reserved on STN
ACCESSION NUMBER: 94:28606 DISSABS Order Number: AAR9418277
TITLE: REGULATION OF MELANOSOME TRANSLOCATIONS IN GOLDFISH MELANOPHORES: EFFECTS OF EPINEPHRINE, ACTH, ATP, LIGHT AND INTRACELLULAR CALCIUM, AND, MOLECULAR CLONING OF THE CDNA FOR A SMALL GTP-BINDING PROTEIN OF GOLDFISH MELANOPHORE
AUTHOR: XIA, YUE [PH.D.]; TAYLOR, JOHN D. [advisor]; TCHEN, T. T. [advisor]
CORPORATE SOURCE: WAYNE STATE UNIVERSITY (0254)
SOURCE: Dissertation Abstracts International, (1993) Vol. 55, No. 2B, p. 271. Order No.: AAR9418277. 134 pages.
DOCUMENT TYPE: Dissertation

FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19940804
Last Updated on STN: 19940804

AB Black moor goldfish melanophore is a classical model to study the regulations of intracellular organelle translocations. I report here that: (A) epinephrine (EP) can induce melanosome aggregation. (1) TMB-8 (an inhibitor of (Ca$\sp{++}$) $\sb{\rm i}$ release) inhibits the effect of EP. Changing extracellular Ca$\sp{++}$ ((Ca$\sp{++}$) $\sb{\rm o})$ concentration from 1 mM to 0.1 μM does not alter the effect of EP suggesting the (Ca$\sp{++}$) $\sb{\rm i}$ release in EP activation. (2) **Adrenergic receptor** (AR) agonists, methoxamine ($\ **alpha**$-1) and clonidine (α-2), are less effective than EP even at 1000 times higher concentration as EP. There is no additive effect with the combination of both agonists. AR antagonists, chloroethy-clonidine (CEC, α-1B, 40 μM) and yohimbine (α-2, IC$\sb{50}$ = 1 nM), block the effect of EP, (3) Pertussis toxin (PTX, 1 μg/ml) does not inhibit EP-induced melanosome aggregation. (4) Amiloride (100 μM), an inhibitor of Na$\sp+$/H$\sp+$ exchanger, can block the effect of EP. These results suggest that the receptor mediating EP-induced melanosome aggregation is a unique α-AR. (B) (1) Complete melanosome dispersion induced by ACTH or forskolin requires 1 mM (Ca$\sp{++}$) $\sb{\rm o}.$ At 0.1 μM (Ca$\sp{++}$) $\sb{\rm o},$ the effect of ACTH or forskolin is only partial implicating a cAMP-modulated (Ca$\sp{++}$) $\sb{\rm o}$ influx. This (Ca$\sp{++}$) influx may be sensitive to ω-**conotoxin** . (2) Extracellular Mg$\sp{++}$-ATP induces a partial melanosome dispersion, apparently requiring (Ca$\sp{++}$) $\sb{\rm o}$ influx. (3) There is a blue light sensitive element(s) that can induce partial melanosome dispersion. (Ca$\sp{++}$) $\sb{\rm o}$ influx is not required for this effect. (C) In order to find gene(s) regulating melanosome translocations, molecular cloning approach was applied. A 1.9 kb (also the size of the mRNA in Northern blot) cDNA J53 is cloned from a cDNA library generated from a goldfish melanophoroma cell line. It is 98.4% homologous to human cdc42 gene, a small G-protein gene, indicating that this protein is highly conserved during evolution. Post-translational analysis of this protein shows potential sites: 1 for myristoylation, 3 for PKC phosphoralytion and 4 for CaM kinase II phosphoralytion, suggesting (Ca$\sp{++}$) $\sb{\rm i}$ may be a major regulator of this protein. The exact function of J53 is unclear.

L66 ANSWER 21 OF 32 CABA COPYRIGHT 2004 CABI on STN
ACCESSION NUMBER: 94:54151 CABA
DOCUMENT NUMBER: 19940501498
TITLE: Evidence of mammalian Ca2+ channel inhibitors in venom of the spider Plectreurys tristis
AUTHOR: Lundy, P. M.; Frew, R.
CORPORATE SOURCE: Pharmacology and Therapeutics, Defence Research Establishment Suffield, Box 4000, Medicine Hat, Alberta T1A 8K6, Canada.
SOURCE: Toxicon (Oxford), (1993) Vol. 31, No. 10, pp. 1249-1256. 25 ref.
ISSN: 0041-0101
DOCUMENT TYPE: Journal
LANGUAGE: English
ENTRY DATE: Entered STN: 19941101
Last Updated on STN: 19941101

AB Plectreurys tristis venom inhibited K+-stimulated Ca2+ influx in a concentration-dependent manner in rat (0.5-4.0 [micro]g venom protein/ml) and chicken (1.0-64.0 [micro]g venom protein/ml) brain synaptosomes. In contrast to Hololena curta venom or omega **conotoxin** GV1A which both show selectivity for avian synaptosomes, inhibition of Ca2+ influx by the venom appeared to be relatively selective for rat synaptosomes. P. tristis venom also inhibited K+-evoked release of [[sup3]H](-)-noradrenaline from labelled rat cortical synaptosomes. Responses to electric field stimulation of the sympathetically innervated rat vas

deferens in vitro were inhibited by P. tristis venom at dilutions similar to those which inhibited Ca2+ influx in synaptosomes. Inhibition persisted following washout of the venom. K+-evoked contractions of rat aortic rings were relaxed by the dihydropyridine antagonist (-)-202-791, but not by P. tristris venom, thus precluding an effect on K+-depolarized smooth muscle L-type channels. Contractions to exogenous (-)-noradrenaline in rat aorta were not inhibited by P. tristris venom, ruling out an effect on [**alpha**]1-**adrenergic receptors**, and
further suggesting a prejunctional site of action. The results suggest that this venom inhibits N-type Ca2+ channels, as well as unclassified Ca2+ channels, which are neither N- nor L-type.

L66 ANSWER 22 OF 32 EMBASE
on STN

ACCESSION NUMBER: 93118809 EMBASE
DOCUMENT NUMBER: 1993118809
TITLE: α-Adrenergic modulation of ionic currents in cultured parasympathetic neurons from rat intracardiac ganglia.
AUTHOR: Xu Z.-J.; Adams D.J.
CORPORATE SOURCE: Molecular/Cellular Pharmacol. Dept., Univ. of Miami School of Medicine,Miami, FL 33101, United States
SOURCE: Journal of Neurophysiology, (1993) 69/4 (1060-1070).
ISSN: 0022-3077 CODEN: JONEA4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB 1. Modulation of ionic conductances by α-adrenergic agonists was investigated in cultured parasympathetic neurons from rat intracardiac ganglia. Application of norepinephrine (NE, 25-100 μM) to the soma of isolated neurons reversibly reduced both the amplitude and duration of the Ca2+-dependent action potential evoked by injection of depolarizing current when Na+ and K+ currents were blocked pharmacologically. 2. In the whole- cell voltage-clamp mode, application of NE reversibly reduced the amplitude and rate of activation of Ca2+ current (I(Ca)). The amplitude inhibition was greater at the peak of the current (55%) than at the end of a 700-ms pulse (20%). Maximal doses of NE produced only .apprx.60% inhibition of peak I(Ca) amplitude. 3. Inactivation of I(Ca) was best fit by the sum of two exponential functions in the absence of NE, but was described by a single exponential function in the presence of NE. These results suggest that NE preferentially inhibited a fast inactivating component of the Ca2+ current in these parasympathetic neurons. 4. NE reversibly reduced the amplitude of Ba2+ tail currents through open Ca channels at all voltages from -40 to +150 mV with a slight shift in the activation curve determined from the current-voltage (I-V) relationship for the tail currents. NE did not change the voltage dependence of the steady-state inactivation of the calcium channels. 5. NE inhibited Ca2+ current either in the absence or presence of nifedipine but to a lesser extent in the presence of ω- **conotoxin** (ω-CGTX),
suggesting that the Ca channels inhibited by NE are predominantly ω-CGTX sensitive. 6. The inhibition of I(Ca) by NE was mimicked by the .**alpha**.**1**- adrenergic agonists methoxamine and
phenylephrine and potentiated in the presence of the α2-**adrenoceptor** antagonist yohimbine (10 μM). NE inhibition of I(Ca) was antagonized by bath application of the α-adrenergic antagonist phentolamine (1 μM), but not by prazosin (1-10 μM), yohimbine, or the β-adrenergic antagonist propranolol (1 μM).
Taken together, these results suggest that NE inhibition of Ca2+ current in rat parasympathetic cardiac neurons is mediated by an α-**adrenergic receptor** with properties that may differ from .**alpha**.**1**- and α2- **adrenoceptors**. 7. In
.apprx.35% of neurons studied, NE not only reduced depolarization-activated inward Ca2+ current but also increased an outward current, with

a shift of the I-V curve and reversal potential to more negative voltages. Replacement of the Cs+ in the pipette by a larger sized cation, arginine, attenuated the NE-induced increase in outward current. This NE-activated current appeared to be a time-independent background current carried by small cations. 8. The inhibition of I(Ca) and activation of background current by NE were mimicked by intracellular application of guanosine-5'-O-(3-thiotriphosphate) (100 μM) and antagonized by either intracellular application of guanosine-5'-O-(2-thiodiphosphate) (100 μM) or pretreatment of the neurons with pertussis toxin. Thus activation of α- **adrenergic receptors** by NE and modulation of I(Ca) and background current is coupled by a pertussis toxin-sensitive G-protein(s). 9. NE-induced inhibition of I(Ca) and activation of background current were not mimicked by activators of adenylate cyclase nor protein kinase activators or inhibitors, suggesting that neither adenosine 3',5'-cyclic monophosphate- protein kinase A nor diacylglycerol (DAG)-protein kinase C second messenger pathways mediate NE modulation of the ionic currents. 10. This modulation of ionic conductances in rat intracardiac neurons by NE may contribute to the positive chronotropic effect observed in the mammalian heart on stimulation of sympathetic nerve terminals.

L66 ANSWER 23 OF 32 EMBASE
on STN

ACCESSION NUMBER: 93297689 EMBASE
DOCUMENT NUMBER: 1993297689
TITLE: Modulation of N-methyl-D-aspartate (NMDA)-stimulated noradrenaline release in rat brain cortex by presynaptic α2-adrenoceptors.
AUTHOR: Fink K.; Gothert M.
CORPORATE SOURCE: Inst. fur Pharmakologie/Toxikologie, Rheinische Friedrich-Wilhelms-Univ., Reuterstrasse 2b,D-53113 Bonn, Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (1993) 348/4 (372-378).
ISSN: 0028-1298 CODEN: NSAPCC
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
023 Nuclear Medicine
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Rat brain cortex slices and synaptosomes preincubated with [3H]noradrenaline were used to investigate whether the NMDA-evoked noradrenaline release is modulated by agonists or antagonists at presynaptic α2- **adrenoceptors**. In experiments on slices, noradrenaline and the preferential α2- **adrenoceptor** agonists talipexole (former B-HT 920) and clonidine inhibited the NMDA-evoked tritium overflow whereas the selective .**alpha**.**1-adrenoceptor** agonists cirazoline and methoxamine were ineffective. The α2- **adrenoceptor** antagonists rauwolscine and idazoxan facilitated the NMDA-evoked tritium overflow whereas the preferential .**alpha**.**1-adrenoceptor** antagonist prazosin was ineffective. The concentration-response curve of talipexole for its inhibitory effect on NMDA-evoked overflow was shifted to the right by idazoxan (apparent pA2 = 7.5). The EC50 of NMDA (97 μmol/l) for its stimulating effect on tritium overflow was not substantially changed by blockade of α2-autoreceptors with 1 μmol/l rauwolscine (EC50 of NMDA in the presence of the α2-**adrenoceptor** antagonist, 155 μmol/l), but the maximal overflow of tritium was increased 2.5 fold by this rauwolscine concentration. In experiments on synaptosomes, talipexole and noradrenaline inhibited the NMDA-evoked tritium overflow. The inhibitory effect of talipexole was abolished by idazoxan which, given alone, was ineffective, as was

prazosin. Talipexole did also not produce an inhibition when tritium overflow was evoked by NMDA in the presence of ω- **conotoxin** GVIA 0.1 μmol/l; the latter, by itself, decreased the response to NMDA by about 55%. It is concluded that the NMDA-evoked noradrenaline release in the cerebral cortex is modulated via presynaptic α2- **adrenoceptors** on the noradrenergic neurones. Stimulation of these autoreceptors in slices by endogenous noradrenaline does not result in a decreased potency of NMDA, but in a decreased maximum effect, in stimulating noradrenaline release. The inhibitory effect of α2- **adrenoceptor** agonists on the NMDA-evoked release is at least partially due to a functional interaction between the NMDA receptors and α2-autoreceptors at the level of the same varicosities. The results obtained with ω- **conotoxin** GVIA suggest that Ca2+ influx via the N-type voltage-sensitive calcium channel (VSCC) occurs in response to NMDA-receptor stimulation and contributes substantially to the induction of NMDA-evoked noradrenaline release. The inhibitory effect of α2- **adrenoceptor** stimulation on this release appears to be ultimately due to an inhibition of the influx of Ca2+ via the N-type VSCC.

L66 ANSWER 24 OF 32 EMBASE
on STN

ACCESSION NUMBER: 90380287 EMBASE
DOCUMENT NUMBER: 1990380287
TITLE: Characterization of a neurogenic and a direct smooth muscle component in the contractile response to electrical field stimulation in rat tail artery.
AUTHOR: Szabo Cs.; Hardebo J.E.
CORPORATE SOURCE: Department of Medical Cell Research, University of Lund, S-223 62 Lund, Sweden
SOURCE: Journal of Autonomic Pharmacology, (1990) 10/5 (283-296). ISSN: 0144-1795 CODEN: JAPHDU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB 1 The extent to which neuronal transmitter release contributes to the contractions induced by transmural nerve stimulation of the rat tail artery at various stimulus intensities was characterized. 2 Using tetrodotoxin, which blocks conduction of the action potential along the nerves, and ω- **conotoxin** GVIA, a blocker of transmitter release from the nerve terminals, as well as chemical and surgical denervations of the perivascular sympathetic nerves, a neurogenic and a direct smooth muscle component could be clearly separated. 3 The neurogenic component was fast in onset, rise and decline (after the end of stimulus), and showed a voltage dependency only at lower stimulus intensities. The non-neurogenic component was slower in onset, rise and decline, and showed a strict voltage dependency throughout the whole stimulus range. This implies that the non-neurogenic component becomes increasingly prominent at high, non-physiological voltages. Mechanisms underlying the declining neurogenic contractile response at the stronger stimulus intensities are discussed. 4 We found no evidence supporting the existence of a possible tetrodotoxin- or ω- **conotoxin** GVIA-resistant contractile component originating from the perivascular nerves (sympathetic or non-symphathetic). Thus, in order to get a purely neurogenic response stimulus intensities should be minimized to give a contraction that is fully sensitive to these two agents. 5 Transmitter release from the perivascular sympathetic nerves was fully responsible for the purely neurogenic contractions. Activation of postjunctional . **alpha.1-adrenergic receptors** was mainly involved, with a substantial contribution from α2-receptors, and a minor contribution from neuropeptide Y receptors. There was no evidence for a contractile component linked to activation of so-called γ- **adrenergic receptors**. 6 β-

adrenergic receptors, serotonergic, cholinergic, prostanoic or purinergic mechanisms do not appear to contribute to the neurogenic (or the non-neurogenic) response. The neurogenic contraction does not utilize potential-sensitive calcium channels.

L66 ANSWER 25 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 14
ACCESSION NUMBER: 1990:158173 BIOSIS
DOCUMENT NUMBER: PREV199089085591; BA89:85591
TITLE: DIFFERENTIAL BLOCKADE BY NIFEDIPINE AND OMEGA **CONOTOXIN** GVIA OF **ALPHA-1** AND BETA-1-**ADRENOCEPTOR**-CONTROLLED CALCIUM CHANNELS ON MOTOR NERVE TERMINALS OF THE RAT.
AUTHOR(S): WESSLER I [Reprint author]; DOOLEY D J; OSSWALD H; SCHLEMMER F
CORPORATE SOURCE: DEP PHARMACOL, UNIV MAINZ, OBERE ZAHLBACHER STR 67, D-6500 MAINZ, FRG
SOURCE: Neuroscience Letters, (1990) Vol. 108, No. 1-2, pp. 173-178.
CODEN: NELED5. ISSN: 0304-3940.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 27 Mar 1990
Last Updated on STN: 10 May 1990
AB Electrically evoked release of [3H]acetylcholine ([3H]ACh) from the rat phrenic nerve and its facilitation by stimulation of presynaptic . **alpha.1**- and β1- **adrenoceptors** were investigated in the absence and presence of nifedipine and ω- **conotoxin** GVIA. Both calcium channel antagonists did not modify electrically evoked [3H]ACh release, but selectively blocked the effect triggered by both facilitatory adrenergic receptors. The increase in [3H]ACh release mediated via β1- **adrenoceptor** activation was abolished by low concentrations (1 nM) of ω- **conotoxin** GVIA, whereas nifedipine (100 nM) abolished the facilitatory effect mediated via .**alpha.1**-**adrenoceptor** stimulation. Therefore, the β1- **adrenoceptor** is apparently coupled to a calcium channel that can be regarded as of the N-type, and the .**alpha.1**-**adrenoceptor** is apparently coupled to a calcium channel that appears as a subtype of the L-type which is not sensitive to ω- **conotoxin** GVIA.

L66 ANSWER 26 OF 32 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 90:74353 SCISEARCH
THE GENUINE ARTICLE: CM293
TITLE: DIFFERENTIAL BLOCKADE BY NIFEDIPINE AND OMEGA-**CONOTOXIN** GVIA OF **ALPHA**-1-**ADRENOCEPTOR**-CONTROLLED AND BETA-1-**ADRENOCEPTOR**-CONTROLLED CALCIUM CHANNELS ON MOTOR-NERVE TERMINALS OF THE RAT
AUTHOR: WESSLER I (Reprint); DOOLEY D J; OSSWALD H; SCHLEMMER F
CORPORATE SOURCE: UNIV MAINZ, DEPT PHARMACOL, OBERE ZAHLBACHER STR 67, W-6500 MAINZ, GERMANY (Reprint); GODECKE AG, FREIBURG, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: NEUROSCIENCE LETTERS, (1990) Vol. 108, No. 1-2, pp. 173-178.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 17

L66 ANSWER 27 OF 32 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1989-23867 DRUGU P
TITLE: Chronic Electroconvulsive Shock and Neurotransmitter Receptors - An Update.

AUTHOR: Gleiter C H; Nutt D J
LOCATION: Bethesda, Maryland, United States
SOURCE: Life Sci. (44, No. 15, 985-1006, 1989) 1 Tab. 159 Ref.
CODEN: LIFSAK ISSN: 0024-3205
AVAIL. OF DOC.: Human Pharmacology Inst., CIBA-Geigy GmbH, Waldhoernlestr. 22, D-7400 Tuebingen, West Germany.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 1989-23867 DRUGU P
AB The effects of ECT on neurotransmitter receptors are reviewed. Effects on beta-, alpha-1- and alpha-2- adrenoceptor, dopamine (DO), 5-HT, GABA + benzodiazepine, ACh, opioid, adenosine and Ca channel receptors in various brain regions and 2nd messenger functions are discussed. The behavioral effects of ECT are related to receptor subtype. Comparisons are drawn with the receptor and behavioral effects of haloperidol, forskolin, zimelidine, desipramine (DE), imipramine, tranylcypromine, paroxetine, mianserin, citalopram, viloxazine, Li, carbachol, carbamazepine and iprindole.
ABEX ECT downregulates beta-**adrenoceptors** (studied using 3H-dihydroalprenolol, noradrenaline (NA) and isoproterenol, reserpine, 6-hydroxydopamine salbutamol, DSP-4, clenbuterol, sertraline, 5,7-dihydroxytryptamine and DE). ECT upregulates some **alpha-1-adrenoceptors** (studied using 3H-prazosin and 3H-WB-4101 binding and phenylephrine). ECT downregulates regional alpha-2-**adrenoceptors** (3H-clonidine and 3H-dihydroergotamine binding). NA turnover is variably affected (3H-DE binding).ECT increases DO function (apomorphine and amphetamine discrimination enhanced motor responses to DB-cAMP, and apomorphine and altered 3H-spiperone and 125I-SCH-23982 binding). ECT upregulates 5-HT-2-receptors (3H-spiperone and 3H-ketanserin binding, HDPAT, forskolin and 1-(3-chlorophenyl)-piperazine), ECT inhibits regional GABA synthesis and its effect on the GABA/benzodiazepine system has been studied using the effect of baclofen on 5-HT release, hypothermia and adenylate cyclase, 3H-GABA, 3H-diazepam and 3H-ethyl-beta-carboline carboxylate binding and sensitivity to DMCM). ACh receptors are downregulated (anterograde amnesia, pilocarpine, arecoline and 3H-QNB binding with and without atropine). Opioid function is altered (morphine, 3H-2-D-Ala,5-D-Leu-enkephalin, 3H-naloxone and 3H-enkephalinamide binding). ECT affects adenosine receptors studied with 2-chloroadenosine, caffeine, 3H-N6-cyclohexyladenosine with and without Gpp(NH)p, 3H-5+-N-ethylcarboxyamideadenosine and 3H-nitrobenzylthioinosine binding). Other drugs include 3H-nimodipine, 3H-nitrendipine and 125I-omega-**conotoxin**, 3H-forskolin and 3H-phorbol 12,13-dibutyrate. (W19/AM)

L66 ANSWER 28 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: AAY92228 peptide DGENE
TITLE: Isolated rho-**conotoxin** peptide used for the treatment of urinary or cardiovascular conditions or diseases, mood disorders or for control of pain or inflammation comprises selective **alpha-1-adrenoceptor** antagonist activity
INVENTOR: Lewis R J; Alewood P F; Sharpe I A
PATENT ASSIGNEE: (UYQU)UNIV QUEENSLAND.
PATENT INFO: WO 2000020443 A1 20000413 47p
APPLICATION INFO: WO 1999-AU843 19991001
PRIORITY INFO: AU 1998-6273 19981002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-303737 [26]
DESCRIPTION: Truncated, inactive rho-contoxin peptide derivative.
AN AAY92228 peptide DGENE
AB The rho-**conotoxin** peptide, rho-TIA (see AAY92227), is isolated from the venom duct of the fish hunting cone snale Conus tulipa. It contains two disulphide bonds. The rho-**conotoxin** peptide has

selective **alpha-1-adrenoceptor** antagonist activity. It can be used in a receptor binding assay to test the activity of a molecule as an antagonist of **alpha-1-adrenoceptor** activity. Rho-TIA is labeled, e.g. with radioactive isotope and used to identify molecules which act at the same site. Antibodies to rho-TIA are useful as therapeutic and diagnostic agents. Rho-**conotoxin** can be used for the treatment of or prophylaxis of a urinary system disease, e.g. prostatic hyperplasia, cardiovascular disease, e.g. arrhythmia, hypertension or coronary heart failure, a mood disorder, e.g. craving (e.g. smoking craving) and pain, e.g. chronic pain, neuropathic pain or inflammatory pain (all claimed).

L66 ANSWER 29 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: AAY92227 peptide DGENE
TITLE: Isolated rho-**conotoxin** peptide used for the treatment of urinary or cardiovascular conditions or diseases, mood disorders or for control of pain or inflammation comprises selective **alpha-1-adrenoceptor** antagonist activity
INVENTOR: Lewis R J; Alewood P F; Sharpe I A
PATENT ASSIGNEE: (UYQU)UNIV QUEENSLAND.
PATENT INFO: WO 2000020443 A1 20000413 47p
APPLICATION INFO: WO 1999-AU843 19991001
PRIORITY INFO: AU 1998-6273 19981002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-303737 [26]
DESCRIPTION: Rho-contoxin peptide, rho-TIA.
AN AAY92227 peptide DGENE
AB The rho-**conotoxin** peptide, rho-TIA, is isolated from the venom duct of the fish hunting cone snale Conus tulipa. It contains two disulphide bonds. The rho-**conotoxin** peptide has selective **alpha-1-adrenoceptor** antagonist activity. It can be used in a receptor binding assay to test the activity of a molecule as an antagonist of **alpha-1-adrenoceptor** activity. Rho-TIA is labeled, e.g. with radioactive isotope and used to identify molecules which act at the same site. Antibodies to rho-TIA are useful as therapeutic and diagnostic agents. Rho-**conotoxin** can be used for the treatment of or prophylaxis of a urinary system disease, e.g. prostatic hyperplasia, cardiovascular disease, e.g. arrhythmia, hypertension or coronary heart failure, a mood disorder, e.g. craving (e.g. smoking craving) and pain, e.g. chronic pain, neuropathic pain or inflammatory pain (all claimed).

L66 ANSWER 30 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: AAA09107 DNA DGENE
TITLE: Isolated rho-**conotoxin** peptide used for the treatment of urinary or cardiovascular conditions or diseases, mood disorders or for control of pain or inflammation comprises selective **alpha-1-adrenoceptor** antagonist activity
INVENTOR: Lewis R J; Alewood P F; Sharpe I A
PATENT ASSIGNEE: (UYQU)UNIV QUEENSLAND.
PATENT INFO: WO 2000020443 A1 20000413 47p
APPLICATION INFO: WO 1999-AU843 19991001
PRIORITY INFO: AU 1998-6273 19981002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-303737 [26]
DESCRIPTION: 3' RACE primer Anchor for rho-TIA gene.
AN AAA09107 DNA DGENE
AB Primer "Anchor" was used with primer rho-1b (AAA09105) to amplify the 3' region of the rho-TIA gene from Conus tulipa. The rho-**conotoxin** peptide, rho-TIA, is isolated from the venom duct of the fish hunting cone snale Conus tulipa. It contains two disulphide bonds. The rho-**conotoxin** peptide has selective **alpha-1-**

adrenoceptor antagonist activity. It can be used in a receptor binding assay to test the activity of a molecule as an antagonist of **alpha-1-adrenoceptor** activity. Rho-TIA is labeled, e.g. with radioactive isotope and used to identify molecules which act at the same site. Antibodies to rho-TIA are useful as therapeutic and diagnostic agents. Rho-**conotoxin** can be used for the treatment of or prophylaxis of a urinary system disease, e.g. prostatic hyperplasia, cardiovascular disease, e.g. arrhythmia, hypertension or coronary heart failure, a mood disorder, e.g. craving (e.g. smoking craving) and pain, e.g. chronic pain, neuropathic pain or inflammatory pain (all claimed).

L66 ANSWER 31 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: AAA09106 DNA DGENE
TITLE: Isolated rho-**conotoxin** peptide used for the treatment of urinary or cardiovascular conditions or diseases, mood disorders or for control of pain or inflammation comprises selective **alpha-1-adrenoceptor** antagonist activity
INVENTOR: Lewis R J; Alewood P F; Sharpe I A
PATENT ASSIGNEE: (UYQU)UNIV QUEENSLAND.
PATENT INFO: WO 2000020443 A1 20000413 47p
APPLICATION INFO: WO 1999-AU843 19991001
PRIORITY INFO: AU 1998-6273 19981002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-303737 [26]
DESCRIPTION: 5' RACE primer AP1 for rho-TIA gene.
AN AAA09106 DNA DGENE
AB AP1 was used with primer rho-1b (AAA09105) to amplify the 5' region of the rho-TIA gene from Conus tulipa. The rho-**conotoxin** peptide, rho-TIA, is isolated from the venom duct of the fish hunting cone snale Conus tulipa. It contains two disulphide bonds. The rho-**conotoxin** peptide has selective **alpha-1-adrenoceptor** antagonist activity. It can be used in a receptor binding assay to test the activity of a molecule as an antagonist of **alpha-1-adrenoceptor** activity. Rho-TIA is labeled, e.g. with radioactive isotope and used to identify molecules which act at the same site. Antibodies to rho-TIA are useful as therapeutic and diagnostic agents. Rho-**conotoxin** can be used for the treatment of or prophylaxis of a urinary system disease, e.g. prostatic hyperplasia, cardiovascular disease, e.g. arrhythmia, hypertension or coronary heart failure, a mood disorder, e.g. craving (e.g. smoking craving) and pain, e.g. chronic pain, neuropathic pain or inflammatory pain (all claimed).

L66 ANSWER 32 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: AAA09105 DNA DGENE
TITLE: Isolated rho-**conotoxin** peptide used for the treatment of urinary or cardiovascular conditions or diseases, mood disorders or for control of pain or inflammation comprises selective **alpha-1-adrenoceptor** antagonist activity
INVENTOR: Lewis R J; Alewood P F; Sharpe I A
PATENT ASSIGNEE: (UYQU)UNIV QUEENSLAND.
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APPLICATION INFO: WO 1999-AU843 19991001
PRIORITY INFO: AU 1998-6273 19981002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-303737 [26]
DESCRIPTION: 5' RACE primer rho-1b for rho-TIA gene.
AN AAA09105 DNA DGENE
AB Primer rho-1b was designed from the mature rho-TIA peptide sequence (AAY92227), a novel **conotoxin**. Rho-1b was used with AP1 (AAA09106) to amplify the 5' region of the rho-TIA gene from Conus

tulipa. The rho-**conotoxin** peptide, rho-TIA, is isolated from the venom duct of the fish hunting cone snale Conus tulipa. It contains two disulphide bonds. The rho-**conotoxin** peptide has selective **alpha-1-adrenoceptor** antagonist activity. It can be used in a receptor binding assay to test the activity of a molecule as an antagonist of **alpha-1-adrenoceptor** activity. Rho-TIA is labeled, e.g. with radioactive isotope and used to identify molecules which act at the same site. Antibodies to rho-TIA are useful as therapeutic and diagnostic agents. Rho-**conotoxin** can be used for the treatment of or prophylaxis of a urinary system disease, e.g. prostatic hyperplasia, cardiovascular disease, e.g. arrhythmia, hypertension or coronary heart failure, a mood disorder, e.g. craving (e.g. smoking craving) and pain, e.g. chronic pain, neuropathic pain or inflammatory pain (all claimed).